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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,953	10/04/2005	William L. Miller	5051-620	2631
20792 7590 12/31/2008 MYERS BIGEL, SIBLEY & SAJOVEC PO BOX 37428 RALEIGH, NC 27627				
EXAMINER BERTOGGIO, VALARIE E				
ART UNIT		PAPER NUMBER		
1632				
MAIL DATE		DELIVERY MODE		
12/31/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/534,953

Applicant(s)

MILLER, WILLIAM L

Examiner

Valarie Bertoglio

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10/14/2007 and 10/24/2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48, 51, 52, 57 and 61-63 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48, 51, 52, 57 and 61-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05/16/2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's reply dated 10/14/2008 and 10/27/2008 are noted. Claims under consideration are claims 48,51-52,57,61-63 dated 10/27/2008. Remarks under consideration are dated 10/14/2008.

Claim Objections

The previous objection to claim 57 is withdrawn in light of Applicant's amendment to the claim.

Claim 57 is newly objected to because of the following informalities: Claim 57 refers to use of the mouse of claim 48. Claim 48 is drawn to a method of making a mouse and is not drawn to the mouse itself. The claim should be amended to read "providing a transgenic mouse made by the method of claim 48". Appropriate correction is required.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48,51-52,57,61-63 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of making a transgenic mouse whose genome comprises a nucleic acid comprising a FSH β -LCR operably linked to a gene encoding a ligand-controllable receptor and separately encoding a Tet operator and minimal promoter operably linked to a gene encoding an ovine FSH β , said method comprising, introducing said nucleic acid in to a mouse fertilized oocyte, implanting said fertilized oocyte into a pseudopregnant female host, obtaining a chimeric offspring from said host and mating the chimera to obtain a transgenic mouse whose genome comprises and expressed the nucleic acid wherein female mice exhibit increased ovulation does not reasonably provide enablement

for the claimed method using 1) any nucleic acid other than that recited above, specifically wherein the gene encoding FSH β is not operably linked to a minimal promoter or 2) for chimeric animals as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's amendments and remarks are fully considered and are partially persuasive. The claims have been narrowed in scope to more clearly define the claimed invention in accordance with the enabled scope given the guidance in the specification. However, aspects of the rejection are maintained for reasons of record as explained below.

Two aspects of the claims remain broad. First, the part of the claimed transgene encoding FSH β is only required to be operably linked to a tet operator response element and a minimal promoter is not required. See page 5, paragraph 4 of the office action dated 06/11/2008). However, the specification has established that a minimal promoter is necessary for expression of the linked transgene (see page 19, paragraph 3). Thus, one of skill in the art would not know how to use the claimed invention without the presence of a minimal promoter because no FSH β would be expressed from the transgene. Applicant has not provided any remarks to this aspect of the rejection.

Second, the claims are not limited to stable germline transgenic mice but encompass founder animals, i.e. mice with genetically different cells wherein some cells comprise the claimed transgene and others do not, and the ratio is variable and undefined. As set forth in the previous office action dated 06/11/2008, claim 48 requires raising the founder animal, which would be chimeric to some degree and, depending on the degree of chimerism in the gonadotropes, the required phenotype may not be obtained. The specification is enabling for increased ovulation in non-chimeric mice whose genome comprises the above set-forth transgene wherein gonadotrope-specific expression is observed.

Applicant argues that it is the chimeric animals that are useful and that these animals are not founders. It appears there may be some misinterpretation of the applied terminology. The chimeric

animals that are deemed not enabled are the founders. When transgenic mice are made by injection of a DNA construct into a fertilized oocyte, not all the cells will necessarily comprise a genome incorporated copy of the transgene. The "founder" mouse made by this method will, as a result, be chimeric. Not all cells will comprise and express the transgene. The ratio of the number of recombinant to non-recombinant cells varies from mouse to mouse. Additionally, which cells comprise the transgene will vary. Thus, the cells that express endogenous FSH- β (a necessary element to start the feedback loop of expression in the claimed recombinant cells) may not comprise the transgene at a high enough ratio even in a mouse having a high percentage of cells comprising the transgene. Applicant argues that it is the chimeric mice that are claimed. In response, the methodology used in making the claimed mice, that of US 6,331,658 and 6,255,554, for example, is methodology in making stable germline transgenics with stable, consistent incorporation of the transgene in the genome of all cells of the animal. It is presumed, given that the specification references these methods as being those used in the instant invention, that the mice described are stable germline transgenics. Stable germline transgenics are the transgenic F1 progeny of the founder chimerics. Not all F1 progeny will be the desired transgenic mice as the germline is chimeric in the founders. However, the desired F1s are easily identified and are assumed to be what is described by the specification.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner
Art Unit 1632